IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TALECRIS BIOTHERAPEUTICS, INC., and BAYER HEALTHCARE LLC,	)	
Plaintiffs,	)	
v.	)	**C.A. No. 05-349-GMS**
BAXTER INTERNATIONAL INC., and BAXTER HEALTHCARE CORPORATION,	)	**Jury Trial Demanded**
Defendants.	)	
BAXTER HEALTHCARE CORPORATION	)	
Counterclaimant,	)	
v.	)	
TALECRIS BIOTHERAPEUTICS, INC., and BAYER HEALTHCARE LLC,	)	
Counterdefendants.	)	

PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

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I. NATURE AND STAGE OF PROCEEDINGS

This is an action for patent infringement brought by Talecris Biotherapeutics, Inc. and Bayer Healthcare LLC (collectively "Plaintiffs") against Baxter International Inc. and Baxter Healthcare Corporation (collectively "Defendants") for infringement of U.S. Patent 6,686,191 ("the '191 patent").[1] Fact discovery in this case closed on September 29, 2006. A hearing on claims construction is scheduled for December 14, 2006. Trial is scheduled to begin July 9, 2007.

This opening claim construction brief is submitted by Plaintiffs pursuant to the Court's Scheduling Order.

II. SUMMARY OF THE ARGUMENT

Plaintiffs' proposed claim construction comports fully with applicable Federal Circuit law and the language of the claims. Plaintiffs' constructions are fully consistent with and supported by the '191 patent specification. As such, Plaintiffs' inventor properly claimed the invention in suit broadly and is entitled to the full scope of the claim language. There are neither words of manifest exclusion or restriction, nor clear disavowel or disclaimer mandating a narrow construction.

Defendants' constructions improperly seek to limit the claims to preferred embodiments and examples, to read limitations from the specification into the claims and to ignore the other language in the claims and claim context.

[1] The parties have agreed that the prosecution history of the '191 patent contained in the Joint Appendix filed herewith (cited as "JA" followed by the page) is the governing copy of the prosecution history for purposes of this case. Particular potions of patents are referenced by column ("col.") and line ("l.").

III. STATEMENT OF FACTS

A. Technological Background of the Claimed Invention

This case involves a method for producing critical, lifesaving antibody drugs. It centers on a novel process for producing immune serum globulin ("ISG") for intravenous administration to a patient.

ISG, also variously known as gamma globulin, immune globulin G and immunoglobulin G (JA145, '191 patent, col.2, l.6), is a highly complex mixture of proteins, predominately of the gamma class of antibodies or IgG, that bind to particular biological targets, or antigens, which are molecules present on bacteria and viruses that may infect a patient. Some of the antibodies in the ISG mixture recognize and bind to antigens on the infecting microorganisms. Antigen binding activates the body's immune system to kill these microorganisms. This infection inactivation system includes a group of proteins collectively called "complement".

ISG therapy is used to treat patients suffering from immune deficiency or who may benefit from supplementation of their own immune system, including patients inflicted with incapacitating, genetically-based immune deficiency diseases and other diseases such as cancer and AIDS. Special versions of immune serum globulins, called hyperimmunes, may be used to treat or prevent diseases such as tetanus, rabies, hepatitis and rH factor incompatibility in pregnant women. *See id.* at col.2, ll.66–67.

Early versions of ISG were administered intramuscularly. Immune globulin intramuscular ("IGIM") therapy is painful and suboptimal. Only limited doses of ISG can be administered at a single injection site and the slow diffusion of ISG from the muscle into the bloodstream compromises rapid system-wide availability of the drug.

Despite these therapeutic challenges, the high incidence of adverse reactions ranging from flu-like symptoms to life-threatening septic shock prohibits intravenous administration of IGIM preparations.

In contrast to IGIM products, immune globulen intravenous ("IGIV") products have the advantage of administration of therapeutically sufficient doses and of virtually instantaneous circulation of ISG throughout the bloodstream.

The adverse reactions seen with early ISG products were associated with decreased serum levels of complement proteins. *Id*. at col.1, ll.17–20. Complement proteins are involved in a cascade of immune reactions that result in the destruction of pathogenic bacteria and other foreign cells. The ability of gamma globulins to bind complement, as specified in the '191 patent, is called anticomplement activity ("ACA"). *Id*. at col.1, 11.19-22. Elevated ACA is undesirable. Indeed, regulatory agencies, including the United States Food and Drug Administration ("FDA"), require that ACA levels of intravenously administerable ISG products be measured and meet regulatory requirements prior to product release.

Since ISG is purified from human blood, it bears risk of transmitting virally-mediated diseases. *Id*. at col.1, ll.45–47. Therefore, in 1991, the Paul-Ehrlich-Institute, which is Germany's equivalent to the Center for Biologics Evaluation and Research ("CBER") within the FDA, issued guidelines requiring a dedicated viral inactivation step as part of the manufacturing process of ISG products. Similar guidelines soon were adopted by the FDA.

B. The Alonso Invention

Dr. William R. Alonso investigated use of a viral inactivation step in the manufacturing process of IGIV. This process, solvent-detergent viral inactivation or "S/D", utilized treatment of ISG with a solvent, tri-n-butyl phosphate or "TNBP," and any of several detergents, to inactivate viruses in the solution without destroying the activity of the ISG proteins. Following a series of experiments treating ISG with TNBP as the solvent and either sodium cholate or polysorbate 80 (also called Tween®-80) as the detergent, Dr. Alonso surprisingly discovered that S/D-treated IGIV failed to meet release specifications because the ACA had elevated and was too high. His discovery is encompassed within paragraph a) of claim 1 of his '191 patent, the patent-in-suit. JA150, '191 patent, col.11, ll.36-39.

Following several months of laboratory research, Dr. Alonso discovered a solution to the ACA problem, namely that using a final incubation step would surprisingly lower ACA to an acceptable level suitable for intravenous administration. Dr. Alonso discovered that the incubation step had the unknown result of lowering the ACA level of an IGIV solution that exhibited elevated ACA as a result of a solvent-detergent treatment step. It is this surprising lowering of ACA levels that is encompassed within paragraph b) of claim 1 of Dr. Alonso's '191 patent. *See* JA150, '191 patent, col.11, ll.40-44.

As claim 1 of the '191 patent details, Dr. Alonso not only discovered the problem -- solvent-detergent treatment results in elevated ACA -- but he also discovered how to solve it -- downstream incubation of the solution under controlled conditions of time, temperature, pH and ionic strength resulted in a lowering of the elevated ACA. The

resulting solution had acceptable ACA levels that were suitable for intravenous administration.

C. The '191 Patent

Claim 1, the only independent claim of the '191 patent, reads as follows:

> A method of treating a solution of antibodies which may have virus activity, the method comprising
>
> a) contacting the solution with a trialkylphosphate and a detergent under conditions sufficient to substantially reduce any virus activity and resulting in an increased level of anticomplement activity; and
>
> b) then incubating the solution of step a) under conditions of controlled time, pH, temperature, and ionic strength, such that the increased anticomplement activity of the solution is reduced to an acceptable level suitable for intravenous administration.

JA150, '191 patent, col.11, ll.34-44.

Claim 1 is followed by 21 dependent process claims and 2 product by process claims.

The "Background" section of the '191 specification describes ACA as "[t]he ability of gamma globulin to bind complement". JA145, '191 patent, col.1, ll.19-21. It then describes in detail the solvent/detergent process of the Neurath patent (see JA48), which is incorporated by reference. *Id.* at 42-54. The specification explains that the S/D process results in ISG preparations with acceptable viral inactivation but with unacceptably high levels of ACA. *Id.* at col.2, ll.6-10.

The "Summary of the Invention" states that the invention is a method for producing an intravenously injectable immune serum globulin (IGIV) "with low anticomplement activity" which has been chemically treated to render it substantially free

of lipid-enveloped viruses. *Id*. at col.2, ll.25-29. The Summary states, "[w]e have discovered that the incubation step is necessary to achieve an acceptable level of ACA low enough to allow the ISG to be administered by intravenous injection". *Id*. at col.2, ll.31-34. The specification later recites that the overriding objective of the described process is to lower ACA such that it is "low enough to be an acceptable level suitable for intravenous administration"; IGIV preparations should have ACA levels as low as possible. JA147, '191 patent, col.5, ll.52-55.

The specification describes specific embodiments such as: (1) solvent/detergent combinations, e.g., TNBP/cholate or TNBP/Tween80, *id*. at col.6, ll.20-66, (2) pH ranges for the incubation step, e.g., JA145, '191 patent, col.1, l.3, (3) time periods for the incubation step, e.g., JA148, '191 patent, col.7, l.42, and (4) temperatures, e.g., *id*. at col.8, l.34.

The specification then expressly states that the disclosure "is intended to illustrate the invention and it is thought that variations will occur to those skilled in the art. Accordingly, it is intended that the scope of the invention should be limited only by the claims below". JA149, '191 patent, col.10, ll.60-63.

IV. BASIC PRINCIPLES OF CLAIM CONSTRUCTION

Claim construction is a matter of law. *Markman v. Westview Instruments, Inc.*, 52 F. 3d 967, 979 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370, 372 (1996). The Court determines the meaning of pertinent claim language to establish the scope of the patent's claims for purposes of determining infringement and validity. *Id.* at 978-79.

Claim construction analysis begins with an examination of the intrinsic evidence, i.e., the claims, specification, and prosecution history of the patent at issue. *Vitronics*

Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). The starting point is the words of the claims, which are presumed to bear their ordinary and customary meaning, as understood by a person of ordinary skill in the art at the time of the invention. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005). The ordinary and customary meaning provides an "objective baseline" from which to begin claim construction. *Id*. at 1313. This objective baseline is informed both by the context in which a term is used in the asserted claim, and by the specification. *Id.* at 1314.

Additionally, as the Federal Circuit stated in *Ormco Corp. v. Align Technology, Inc.*, 463 F.3d 1299 (Fed. Cir. 2006), "'[W]e have repeatedly warned against confining the claims to [the disclosed] embodiments'" (quoting *Phillips*, 415 F.3d at 1323). While an inventor may use the specification to intentionally disclaim or disavow the broad scope of a claim, *Phillips*, 415 F.3d at 1316, this intention must be clear, *see Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313, 1325 (Fed. Cir. 2002) ("The patentee may demonstrate an intent to deviate from the ordinary and accustomed meaning of a claim term by including in the specification expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope."). It is improper to draw limitations into the claim from a preferred embodiment, *see Phillips*, 415 F.3d at 1323 ("[W]e have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment."). Further, "when a claim term is expressed in general descriptive words, we will not ordinarily limit the term to a numerical range that may appear in the written description or in other claims." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d

1243, 1249 (Fed. Cir. 1998); *see Conoco Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1357-58 (Fed. Cir. 2006).

Under 35 U.S.C. § 112, ¶ 4, "[A] claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers." *See AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1242 (Fed. Cir. 2003) ("Under the doctrine of claim differentiation, dependent claims are presumed to be of narrower scope than the independent claims from which they depend.") Moreover, as set forth in *Phillips*, 415 F.3d at 1315, "[t]he presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *See also Free Motion Fitness, Inc. v. Cybex Int'l*, 423 F.3d 1343, 1351 (Fed. Cir. 2005) ("The doctrine of claim differentiation 'create[s] a presumption that each claim in a patent has a different scope.' The difference in meaning and scope between claims is presumed to be significant '[t]o the extent that the absence of such difference in meaning and scope would make a claim superfluous.'") (citations omitted).

The specification is also relevant to claim construction analysis. In instances where claim terms are unclear, the specification is the single best guide to the meaning of a disputed claim term. *Id.*, citing *Vitronics*, 90 F.3d at 1582. While the specification undoubtedly serves as a guide to claim construction, the Federal Circuit has repeatedly cautioned against importing limitations from the specification into the claims. *Phillips*, 415 F.3d at 1312 (stating that it is a "'bedrock principle' of patent law that 'the claims of a patent define the invention' … [and thus] '[t]he written description part of the

specification itself does not delimit the right to exclude. That is the function and purpose of the claims.'") (citations omitted). In addition, mere description in the specification that an invention will be used in a particular way does not so limit an invention, absent a "clear disclaimer" of particular subject matter. *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 909 (Fed. Cir. 2004).

Resort may also be made to extrinsic evidence, such as expert testimony and dictionaries, if needed to assist in determining the meaning or scope of technical terms in the claims. *Id.* at 1583. Since such sources are potentially less reliable in interpreting claim scope than the intrinsic evidence, the Federal Circuit has endorsed the use of extrinsic evidence only when it serves as an aid "to help educate the court regarding the field of the invention" and "determine what a person of ordinary skill in the art would understand claim terms to mean." *Phillips*, 415 F.3d at 1319.

The Federal Circuit has explained that "[a] patentee may claim an invention broadly and expect enforcement of the full scope of that language absent a clear disavowal or contrary definition in the specification." *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004). Therefore, claims written more broadly than the specific embodiments disclosed in the specification are not limited to those embodiments. *Liebel-Flarshiem*, 358 F.3d at 906. Relatedly, limitations from parts of the patent outside the claims cannot be imported to limit the scope of the claims "unless the language of the claims invites reference to those sources." *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 989-90 (Fed. Cir. 1999); *Elector Medical Sys., S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1054 (Fed. Cir. 1994).

V. INTERPRETATION OF THE '191 PATENT CLAIMS

Plaintiffs have presented their proposed claim constructions on all the terms at issue in this case in the Joint Claims Construction Chart. Plaintiffs contend that nearly all of the contested terms should simply be accorded their ordinary meaning, and routinely advance the ordinary meaning of the terms, and demonstrate support for such from the patent claim language *per se*. In contrast, Defendants repeatedly seek to limit the terms in violation of Federal Circuit law. They urge the Court to re-write the claims by reading extraneous terms, preferences, examples and limitations from the specification into the claims. The Federal Circuit has mandated that such an approach is improper absent "words or expressions of manifest exclusion or restriction." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1324 (Fed. Cir. 2002).

A. The Term "Any Virus Activity" Should Be Accorded Its Ordinary Meaning – Contrary to Defendants' Position, "Any" Does Not Mean "All"

In context, claim 1 recites "under conditions sufficient to substantially reduce **any virus activity**."[2] The term "any virus activity" needs no construction and is clear on its face. It is equally clear from the language of the claim that "any virus activity" is part of the language specifying the first requirement for the recited "conditions"; that they provide a substantial reduction in the activity of *any* of the many potential viruses that may be present, and not "*all* virus activity," as proposed by Defendants. In other words, "any virus activity" means "any virus activity which is substantially reduced by the conditions of step a)." The ordinary meaning is fully consistent with the specification, which explicitly teaches that the "conditions" of the solvent/detergent treatment are not

[2] Throughout this brief Plaintiffs' proposed constructions are bolded at the beginning of each section.

intended to remove "*all* virus activity". Indeed, as we explain below, the specification incorporates by reference the Neurath '573 patent which explains in detail the viral inactivation process and describes the virus activity that is substantially reduced thereby.

We note that the ordinary meaning of "any virus activity" is equally consistent with the preamble of the claim, which demonstrates that virus activity is not necessarily present in the first place. Indeed, the preamble for claim 1 recites "[a] method of treating a solution of antibodies which *may* have virus activity, the method comprising…" (emphasis added). The preamble contradicts Defendants' construction. "'[I]f the preamble helps to determine the scope of the patent claim, then it is construed as part of the claimed invention.'" *Seachange Int'l, Inc. v. C-COR Inc.*, 413 F.3d 1361, 1375-76 (Fed. Cir. 2005) (citations omitted); *see also Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615, 620 (Fed. Cir. 1995) ("[A] claim preamble has the import that the claim as a whole suggests for it."). Under the preamble, the solution *may* have virus activity, or it may not. The preamble makes clear that claim 1 does not require substantial reduction of the activity of all viruses in solution.

Defendants posit a construction at odds with the term's plain and ordinary meaning by seeking to re-write the claim and to convert "any" to "all". According to Defendants, "any virus activity" means "activity of *all* viruses in solution." Thus, Defendants propose a construction which one skilled in the art, reading the '191 specification and '573 Neurath patent, would know is inaccurate, and which could artificially create issues of alleged inoperability.

It is clear from the specification that the "conditions" of the S/D treatment are not intended to remove *all* virus activity, as exemplified by the citations relied on by

Defendants. The specification speaks of "virus inactivation" (*see* JA145, '191 patent, col.1, l.8-12; *id*. at col.2, l.6-10; JA146, '191 patent, col.3, ll.65-67), but not in the context of inactivating *all* viral activity, as Defendants suggest. Defendants cite to part of a sentence discussing the "[i]nactivation of viruses" (*see* JA145, '191 patent, col.1, l.42-45). They fail to cite the remaining part of the sentence (*see id.* at col.1, l.45-47), which incorporates by reference the viral inactivation process of Neurath where inactivation of lipid-enveloped viruses is but one embodiment. (*See* JA48-59, '191 patent, col.1, ll.9-10) ("[T]his invention relates to the inactivation of viruses, especially lipid-enveloped viruses, e.g., hepatitis B."). Incorporation by reference of an issued patent integrates the prior art into the specification and renders the prior art intrinsic evidence. *Advanced Display Sys., Inc. v. Kent State Univ.*, 212 F.3d 1272, 1282 (Fed. Cir. 2000) ("Incorporation by reference provides a method for integrating material from various documents into a host document . . . by citing such material in a manner that makes clear that the material is effectively part of the host document as if it were explicitly contained therein.").

Defendants also cite to an embodiment providing for "maximum viral inactivation" at certain conditions (*see* JA146, '191 patent, col.4, l.21-24), and another embodiment providing for "accelerated" inactivation of two types of viruses at certain conditions (*see id*. at col.4, l.24-29). These embodiments make it clear that inactivation of *all* viruses in solution is not contemplated by the invention or suggested by the specification. Rather, the "conditions" are used to inactivate certain types of viruses.

Defendants proposed construction is unsupportable and should be rejected.

B. The Term "Under Conditions Sufficient To Substantially Reduce Any Virus Activity And Resulting In An Increased Level Of Anticomplement Activity" Should Be Accorded Its Ordinary Meaning – Defendants Misstate The Claim Language And Again Contravene Federal Circuit Law

The parties first disagree about what words of claim 1 should be addressed. Defendants offer a construction for cropped terms that do not appear in claim 1. "Under conditions . . . resulting in an increased level of ACA" is devoid of context and thus contrary to the rule that it is impermissible to ignore claim language during construction. *See BBA Nonwovens Simpsonville, Inc. v. Superior Nonwovens, LLC*, 303 F.3d 1332, 1344 (Fed. Cir. 2002) (rejecting infringer's construction that ignored the word "positioned" in a means-plus-function claim).

The complete term "under conditions sufficient to substantially reduce any virus activity and resulting in an increased level of ACA," is clear on its face and requires no construction. It means what it says: **those conditions that are sufficient to substantially reduce any virus activity and result in an increased level of ACA**.

Defendants' proffered claim construction violates at least three tenets of patent law: (1) it reads preferred embodiments into the claim; (2) it ignores dependent claims and the doctrine of claim differentiation; and (3) it excludes preferred embodiments from the claim.

First, Defendants improperly read several limitations into the claim by requiring the use of one specific solvent - TNBP; one specific detergent - cholate; and a single pH condition, pH of about 7.0. As stated, it is improper to import limitations where they do not exist in the claims. *SanDisk Corp. v. Memorex Prods., Inc.*, 415 F.3d 1278, 1286

(Fed. Cir. 2005) ("'References to a preferred embodiment, such as those often present in a specification, are not claim limitations.'")(citations omitted).

Defendants' references to the specification only confirm their errors. At col.3, l.62 through col.5, l.41, the '191 specification exemplifies preferred embodiments which Defendants impermissibly attempt to import into the claim. JA146-147. At col.6, ll.26-63, the '191 specification again exemplifies preferred embodiments in the form of text and tabulated experimental data. JA147. At col.8, ll.6-9 and 10, the specification exemplifies an experiment using TNBP and cholate and a pH of 7.0, the very embodiment upon which Defendants rely for their impermissibly limited claim construction. JA148. Finally, Defendants cite experimental data in Tables 1, 5, 6, and 7 in their effort to import examples into the claim. Attempting to limit the claim by reading preferred embodiments and examples into it is improper. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002); *see Phillips*, 415 F.3d at 1323 (claims are not to be construed as being limited to the described embodiments); *see also SanDisk*, 415 F.3d at 1286 ("'References to a preferred embodiment, such as those often present in a specification, are not claim limitations.'") (citations omitted).

Second, Defendants' construction violates another rule: it would result in independent claim 1 being narrower than dependent claims 19 and 20. Claim 19 is dependent from claim 1 and specifies that the detergent is selected from polysorbate 80 and sodium cholate. Consequently, claim 1 must include polysorbate 80, sodium cholate, and other detergents. Defendants' proffered claim construction would therefore violate 35 U.S.C. § 112, ¶ 4 and fundamental case law requiring dependent claims to be narrower than the independent claims from which they depend. 35 U.S.C. § 112, ¶ 4, *supra; AK*

Steel Corp., 344 F.3d at 1242 ("dependent claims are presumed to be of narrower scope than the independent claims from which they depend."). Defendants commit the same error by construing claim 1 to require a pH of about 7.0. Claim 20, which depends from claim 1, specifies a pH of between about 3.5 and about 6.0, and thus necessitates that the pH range of independent claim 1 be greater than between about 3.5 to about 6.0. Defendants' suggested pH for claim 1 is not even within the pH range in dependent claim 20.

Finally, Defendants' construction would impermissibly exclude a preferred embodiment from claim 1. *Pfizer, Inc. v. Teva Pharms., USA, Inc.*, 429 F.3d 1364, 1374 (Fed. Cir. 2005) ("A claim construction that excludes a preferred embodiment…is 'rarely, if ever, correct.'") (*quoting Vitronics*, 90 F.3d at 1583) (citation omitted). The specification clearly teaches that "better virucidal activity was observed at pH values less than 6.0." JA148, '191 patent, col.8, ll.39-40. Moreover, the specification teaches that "material incubated at pH 5.8 had lower ACA levels than the pH 7.0 samples…." *Id*. at col.8, ll.41-42. As such, to limit the claim to pH 7.0 would exclude the very embodiments of the invention that the specification teaches produce the best results.

For the reasons cited above, Defendants' proposed construction of this term should be rejected.

C. The Term "Increased Level Of Anticomplement Activity" Should Be Given Its Ordinary Meaning – Defendants' Continued Effort To Read Limitations Into The Claim, In This Instance By Adding The Word "Unacceptable", Should Be Rejected

This term requires no construction. The ordinary meaning of "increased level of anticomplement activity" is simply an **anticomplement activity level which increases**

as a result of contacting the solution with a solvent and detergent. It is not possible to add clarity to this term or to construe it in any other way. In other words, "increased level of anticomplement activity" means "an anticomplement activity level that increases as a result of contacting the solution with a solvent and detergent."

Conversely, Defendants attempt to import a novel limitation into the claim. They state that "increased level of ACA of the solution" means "increased ACA *from a level acceptable* for intravenous administration *to a level unacceptable* for intravenous administration" (emphasis added). This construction is devoid of support. It is inconsistent with the claim language itself, the specification, and the prosecution history. Defendants' citations expose their construction for what it is – a blatant effort to read stringent limitations into the claim.

First, step (a) of claim 1 says nothing about "acceptability" of ACA levels. Yet, Defendants are improperly attempting to read acceptability/unacceptability limitations into this part of the claim. *See Phillips*, 415 F.3d at 1312.

Second, the '191 specification does not require that ACA levels be unacceptable at any time. All of Defendants' citations to the specification speak of ACA levels being acceptable or unacceptable, but not a single one requires, or even implies, that ACA levels *increase* from acceptable to unacceptable levels at any point in the process.[3]

[3] JA143, '191 patent, Abstract (ACA is "reduced to an acceptable level," but no mention that ACA is increased "from" an acceptable level); JA145, '191 patent, col.2, l.6-18 (discussing unacceptably high ACA levels in prior art processes, but not requiring that the '191 invention increases to an unacceptably high ACA); *Id*. at col.2, l.31-34 (incubation step is necessary to achieve an acceptable level of ACA low enough to allow for intravenous administration, but no requirement whatsoever for ACA levels to be unacceptable prior to incubation); JA147, '191 patent, col.5, l.47-49 ("[e]levated ACA levels" detected at a particular processing step, but no mention of ACA levels increasing from an acceptable level to an unacceptable level); JA148, '191 patent, col.7, l.20-24 (discussing how prior art processes yielded ACA levels unsuitable for intravenous administration); JA149, '191 patent, col.9, l.38-44 (data in the patent suggest an embodiment, i.e., that the invention can be used to make S/D-treated solutions with undesirable

Equally important, the experiments described in the specification demonstrate that such a construction was not contemplated by the inventors. In column 5, ll.57-64 of the '191 patent, the patentees describe preferred ACA levels that are suitable for intravenous administration. JA147. Specifically, a preferred ACA level for a 5% IGIV solution is less than 45 CH_{50} units/mL, and a preferred ACA level for a 10% IGIV solution is less than 60 CH_{50} units/mL. *Id*. Contrary to Defendants' asserted claim construction, Table 7 of the '191 patent shows that three of the four 5% solutions subjected to the claimed incubation of step b) had pre-incubation (post-S/D treatment) ACA values that were already less than the preferred ACA level. This ACA level was subsequently decreased by the claimed incubation to a lower value. Similarly, two of the three 10% solutions had pre-incubation (post-S/D treatment) ACA values less than the preferred ACA levels, and these too were lowered by the subsequent incubation.

The described invention teaches that the desired ACA values be as low as possible, and even if the initial values are already suitable for intravenous administration further lowering is still contemplated. *Id*. at col.5, ll.51-55 ("While there is no strict rule for determining when the ACA level is low enough to be an acceptable level suitable for intravenous administration, IGIV preparations should have ACA values *as low as possible*")(emphasis added). Any claim construction that requires the S/D treatment to increase the ACA to levels that are "unacceptable" is thus directly contradicted by the teachings of the specification.

ACA levels suitable for intravenous administration); *Id*. at col.10, l.24-26 (discussing how prior art processes yielded unacceptable ACA levels).

Third, Defendants' citations to the prosecution history do not mandate that ACA levels must always be unacceptable. Defendants' citations to the prosecution history seize every mention of the words "acceptable" and "undesirable". Defendants fail to realize that these words were illustratively used in discussions regarding whether combining the prior art would have been obvious to Dr. Alonso. They were not used to limit the claims.

It is axiomatic that the claim language defines the scope of the claimed invention. The claim language clearly does not require levels to be unacceptable at any point in the process. Defendants' attempt to import such a limitation is improper. *Phillips*, 415 F.3d at 1312.

To summarize, Defendants are repetitively attempting to import time- and value-limitations into the claim. *See SanDisk*, 415 F.3d at 1286 ("'References to a preferred embodiment, such as those often present in a specification, are not claim limitations.'") (citations omitted). Defendants desire the word "increased" to mean that the ACA level start at an acceptable value, and rise to an unacceptable value. But the '191 claims do not contain this limitation. This construction is contrary to the plain meaning of the term "increased level of ACA." Defendants' proposed construction is also in direct contrast to the experiments described in the specification, which clearly show pre-incubation (post-S/D) values below preferred embodiments for acceptable ACA levels suitable for intravenous administration. The Court should therefore reject Defendants' proposed construction and adopt the ordinary meaning of the claim language.

D. The Term "Anticomplement Activity" Means The Ability Of Antibodies To Bind Complement

The term "anticomplement activity" ("ACA") appears in asserted claim 1. The patentee provided an explicit definition of ACA in the specification: "**the ability of antibodies to bind complement**." *See* JA145, '191 patent, col.1, ll.9-22 ("The ability of gamma globulin to bind complement"). The words used to define ACA are words commonly used and understood in the art, and a skilled artisan would know exactly what the definition means. Defendants professed inability to understand what "ACA" means flies in the face of the '191 specification and well-known FDA regulation of ACA.

Ignoring the clear definition in the specification, Defendants offer their own definition for ACA: "The amount of protein capable of activating 50% of the complement in an optimally titered complement and red blood cell/hemolysin system, as determined by the particular ACA assay used to obtain the ACA data reported in the '191 patent." Defendants' definition is flawed for at least three reasons. First, as previously discussed, the definition is contrary to both the plain meaning of ACA and the definition ascribed by the patentee. Second, the definition lacks proper support in the specification. Third, the definition improperly requires the use of a particular measuring technique (i.e., "assay") to the exclusion of all other measuring techniques. ACA is a scientific term and it can be measured in a variety of different ways and expressed in different units. Claim 1 specifies neither units nor measurement techniques.

Defendants selectively quote from a portion of the specification which defines, not ACA, but "one unit of ACA (one CH_{50} unit)." JA147, '191 patent, col.5, l.64-col.6, l.1. Defendants thus read CH_{50} into the claim when it is not there and attempt to persuade

the Court that ACA means one *unit* of ACA. One unit of ACA activity (one CH_{50} unit) is clearly not equal to ACA, just as one *unit* of length (one meter) is not equal to length. The unit is merely one particular way of expressing ACA, but not the only way. By way of analogy, Defendants would reject that "length" means "the distance between two points," and would instead propose that "length" means "one meter."

Defendants next cite the first two sentences of the Background section but notably exclude the third sentence, wherein the definition of ACA is clearly and explicitly provided. *See* JA145, '191 patent, col.1, ll.20-22. Blatantly avoiding the clear definition of ACA belies Defendants' assertion that ACA "is not susceptible to a sufficiently precise definition." Defendants also cite to other passages in the specification which fail to support their proposed construction. *See id.* at col.1, ll.15-19 (referring to "complement binding") and *id*. at col.2, ll.15-17 & 31-34 (referring to ACA levels consistent with "the ability of antibodies to bind complement").

Defendants' construction also impermissibly mandates a particular measuring technique be used to the exclusion of all others, again importing limitations from the specification into the claims. *Phillips*, 415 F.3d at 1312.

E. The Term "Then Incubating The Solution Of Step a)" Is Clear On Its Face And Means "Incubating The Solution That Originates From Step a)" – Defendants' Attempt To Preclude Additional Processing Steps Is Contrary To The Claim Language "Comprising" And The Specification

The term "then incubating the solution of step a)" should be defined as "**incubating a solution originating from step a) under conditions of controlled time, pH, temperature, and ionic strength, wherein additional steps may be performed prior to said incubating**." Such a construction is clear from the ordinary meaning of the claim language and the specification. *See Phillips*, 415 F.3d at 1313 ("the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.").

Defendants assert that this term should mean "incubating the solvent-detergent treated solution resulting from step a) without any additional processing steps between steps a) and b)." (Emphasis added). Such a construction directly contradicts the claim language, the specification and the stated purpose of the patent. The specification clearly contemplates additional processing steps between step a) and step b). Moreover, the title of the patent is directed to producing a product that can be administered by intravenous injection, which requires additional processing steps between claimed steps a) and b).

First, the claim language employs the open-ended transitional phrase "comprising", which signals the public that the claimed method is open to additional steps. Exhibit A, MPEP § 2111.03 (8th ed., Rev. 5, Aug. 2006); *see Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1350 (Fed. Cir. 2003). If the patentee had intended the claim to exclude other steps, the patentee would

have used the closed transitional phrase "consisting of." *See PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). Defendants fail to appreciate this distinction and ask this Court to equate "comprising" and "consisting of". Very plainly, "comprising" is open to additional steps.

Not only does the claim language allow for additional steps between step a) and step b) of claim 1, the specification also clearly teaches specific additional steps such as sterile filtration and tonic adjustment. The specification states that after removing the solvent and detergent from the solution, "the ISG preparation is adjusted to 5% or 10% protein, and treated to render it tonic, *i.e.*, to render it compatible with physiological conditions, or render it physiologically acceptable…." *See* JA147, '191 patent, col.5, ll.25-41. The specification also states that the experiments described in the patent were performed on "sterile bulk," which requires sterile filtration between claimed steps a) and b) of the patent. S*ee* JA145, '191 patent, col.2, ll.10-23; JA148, '191 patent, Table 5; JA149, '191 patent, Table 7; JA148, '191 patent, col.8, ll.29-37. *See also* JA149, '191 patent, col.9, ll.11-21. As such, it is clear that the patentee contemplated the inclusion of additional processing steps between the viral inactivation steps and the incubation steps.

Plaintiffs' construction is thus entirely consistent with how one of ordinary skill in the art would interpret this language, particularly in view of the overall purpose of the claimed invention, as described by the specification – to prepare virally inactivated immune serum globulin suitable for intravenous injection.

F. The Term "Increased Anticomplement Activity Of the Solution" Is Clear And Unambiguous

The term "increased anticomplement activity of the solution" should be given its ordinary meaning. It needs no construction. It is clear on its face. As discussed above, "ACA" is defined in the specification. This term therefore simply means **an increase in the ACA levels of a solution as a result of contacting the solution with a solvent and detergent**. In other words, "increased anticomplement activity of the solution" means "an anticomplement activity level that increases as a result of contacting the solution with a solvent and detergent."

Defendants' proffered construction fails on a number of grounds.

First, Defendants attempt to vitiate the ordinary meaning of this term by dividing it into "increased anticomplement activity" and "of the solution." Defendants argue that "increased anticomplement activity" means "increased anticomplement activity from a level acceptable for intravenous administration to a level unacceptable for intravenous administration." This is the same erroneous definition that Defendants assert for the term "increased anticomplement activity of the solution." For the same reasons stated above, Defendants' proffered definition is inconsistent with the claim language, the specification, and the prosecution history.

Second, Defendants argue that "of the solution" is indefinite. They are wrong. By parsing out the phrase "of the solution" from "increased anticomplement activity of the solution," and the remainder of step (b) of claim 1, Defendants seek to confuse the meaning of this term which is otherwise clear on its face. In construing claims, courts "must give each claim term the respect that it is due." *Pause Tech., LLC v. TiVo Inc.*, 419

F.3d 1326, 1334 (Fed. Cir. 2005); *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir.), *cert. denied*, 126 S. Ct. 488 (2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."). Here, the "solution" clearly refers to the "solution" that is to be incubated, i.e., the solution from step (a) that is to be incubated. As we have shown above, this solution may have been treated with post-SD, pre-incubation processing steps.

In the alternative, Defendants assert that this term means "increased anticomplement activity of the solution from a level acceptable for intravenous administration to a level unacceptable for intravenous administration." Again, Defendants are seeking to contort the plain meaning of the claim by equating the word "increased" with unacceptability of anticomplement activity levels. Such a construction has no basis in claim language, specification, or the prosecution history, for the reasons cited previously.

G. The Term "Acceptable Level Suitable for Intravenous Administration" Is Clear And Unambiguous

The term "**acceptable level suitable for intravenous administration**" should be given its ordinary meaning. This term needs no construction because it is clear on its face. A person of ordinary skill in the art would know that when intravenously injecting immune serum globulins into a patient, ACA has to be at an acceptable level.

Elevated ACA is undesirable, as it has been associated with various adverse events in patients. As a result of these potential health concerns related to elevated ACA levels, manufacturers of IGIV products desire to have ACA levels that are as low as possible, within the realm of available manufacturing technologies. JA147, '191 patent,

col. 5, 11.51-55. Even if an ACA level value is technically lower than the FDA's upper limit for product release, it is still desirable to reduce the ACA level to the lowest value possible. By analogy, even if pollution levels in the atmosphere meet the minimum acceptable levels, it is still desirable to lower atmospheric pollution to the lowest levels possible.

Regulatory agencies, including the FDA, require that ACA levels be measured and meet regulatory requirements prior to the product release. There are multiple methods for measuring ACA which would be known to one of ordinary skill in the art, and some of which have been published by the U.S. CDC and the European Pharmacopeia for use by manufacturers. Accordingly, one of ordinary skill in the art would readily recognize that "acceptable level suitable for intravenous administration" means an ACA level suitable for release under applicable standards, including standards set by regulatory agencies as well as the manufacturer's internal release standards.

Defendants take the position that this term is indefinite. This argument is flawed. "The definiteness requirement of § 112, ¶ 2, 'focuses on whether the claims, as interpreted in view of the written description, adequately perform their function of notifying the public of the [scope of the] patentee's right to exclude.'" *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1338 (Fed. Cir. 2003) (citations omitted). Not only would a skilled artisan know that ACA has to be at an acceptable level before injecting immune serum globulins into a patient's arm, but the specification gives numerous examples of acceptable levels of ACA suitable for intravenous administration. *See id*. at col.5, ll.51-63.

Defendants then resort to the examples and read them into the claim, taking the position that this term means "a defined numerical level that depends upon the protein concentration, specifically, 60 CH_{50} units/mL for a 10% solution and 45 CH_{50} units/mL for a 5% solution, as determined by the particular anticomplement assay used to obtain the anticomplement activity data reported in the '191 patent." By their construction, Defendants once again are improperly limiting the claim to examples and preferences, and importing limitations from the abstract and specification into Claim 1.

The abstract states a preferred embodiment for what would be an acceptable level of ACA suitable for intravenous administration. *See* JA143, '191 patent, Abstract ("In a preferred embodiment, the anticomplement activity is reduced to less than 60 CH_{50} units/mL...."). Defendants reference the abstract in support of their construction, but it is well-established that mere citation to a preferred embodiment is insufficient to effect a disavowal of claim scope. *CCS Fitness*, 288 F.3d at 1366. *See Phillips*, 415 F.3d at 1323 (claims are not to be construed as being limited to the described embodiments); *see also SanDisk*, 415 F.3d at 1286 ("'References to a preferred embodiment, such as those often present in a specification, are not claim limitations.'") (citations omitted).

The specification also discusses preferred ACA levels that are acceptable levels of ACA suitable for intravenous administration. *See* JA147, '191 patent, col.5, ll.51-63. ("For a 5% ISG formulation the acceptable level suitable for intravenous administration ***preferably*** would be less than about 45 CH_{50} units/mL, and ***more preferably*** less than about 30 CH_{50} units/mL. For a 10% ISG formulation, the acceptable level suitable for intravenous administration ***preferably*** would be less than about 60 CH_{50} units/mL, and ***more preferably*** less than about 45 CH_{50} units/mL.") This portion of the specification

relates only to preferred embodiments. Defendants are improperly attempting to import these preferred embodiments into the claim. *See, e.g., Agfa Corp. v. Creo Prods., Inc.*, 451 F.3d 1366, 1376 (Fed. Cir. 2006) ("This case illustrates again the reason for this court's refusal to limit broader claim language to a preferred embodiment in the patent specification.").

Rather than contort this claim by seeking to rewrite it, this term should simply be accorded its ordinary meaning, with no further construction required.[4]

H. "Ionic Strength"

Plaintiffs and Defendants have reached agreement on the construction of "ionic strength."

Term No.	Asserted Claim(s)	Term	Agreed Construction
1	1,10,12, 23	"ionic strength"	"ionic strength" means "the summation: $I=\frac{1}{2}\Sigma(c_i z^2)$ where c_i is the concentration of each type of ion (in moles 1^{-1}) and z is its charge.

[4] Plaintiffs have elected to withdraw claims 5 and 6, and therefore no construction of "about 60 CH_{50} units" or "about 45 CH_{50} units" is needed.

VI. CONCLUSION

For the foregoing reasons, we respectfully submit that the interpretation of the claims urged by Plaintiffs should be adopted by the Court. Plaintiffs' proposed constructions most closely comport with the language of the claims, the specification, and applicable law.

Respectfully submitted,
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CERTIFICATE OF SERVICE

I, hereby certify on this 27th day of October, 2006 I electronically filed the foregoing PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF with the Clerk of Court using CM/ECF which will send notification of such filing to the following:

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